

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. – 10. (Cancelled).

11. (Currently amended) A method of making an MR imaging agent, said method comprising:

a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;

b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent;

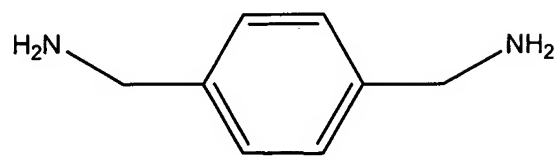
c) converting the precursor MR imaging agent to the MR imaging agent;  
wherein converting the precursor MR imaging agent to the MR imaging agent comprises:

(d) reacting the precursor MR imaging agent with a precursor chelate moiety to form a covalent bond between the precursor chelate moiety and the linker moiety of the precursor MR imaging agent, the precursor chelate moiety comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;

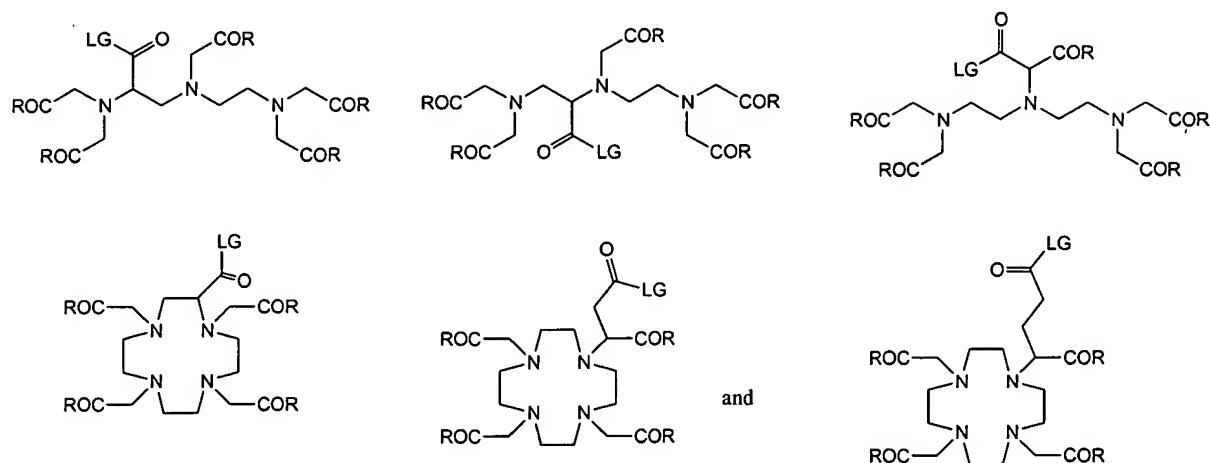
(e) transforming a plurality of the carboxylate precursor groups of the bound precursor chelate moiety to a plurality of carboxylate moieties, the carboxylate moieties capable of complexing a paramagnetic metal ion; and

(f) complexing a paramagnetic metal ion to the plurality of carboxylate moieties to produce the MR imaging agent;

wherein the linker-subunit moiety is:



~~The method of claim 8~~, wherein the precursor chelate moiety is selected from the group consisting of:



wherein LG is a leaving group selected from the group consisting of -OH, activated ester, halide, and anhydride, and wherein each R, independently, is an O<sup>-</sup> or an O<sup>-</sup> precursor selected from the group consisting of OH, -O-Me, O-Et, O-tBu, O-benzyl, and O-allyl, so that R, upon conversion to O<sup>-</sup>, is capable of forming a carboxylate moiety with its adjacent carbonyl.

12. – 13. (Cancelled).

14. (Currently amended) A method of making an MR imaging agent, said method comprising:

a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;

b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent;

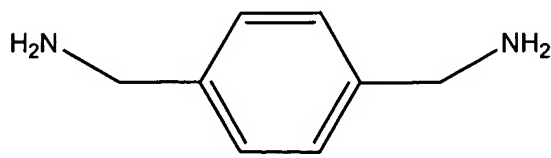
c) converting the precursor MR imaging agent to the MR imaging agent;  
wherein converting the precursor MR imaging agent to the MR imaging agent comprises:

(d) reacting the precursor MR imaging agent with a precursor chelate moiety to form a covalent bond between the precursor chelate moiety and the linker moiety of the precursor MR imaging agent, the precursor chelate moiety comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;

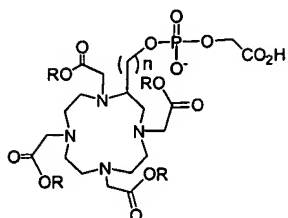
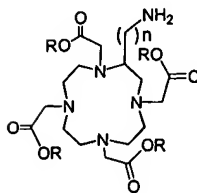
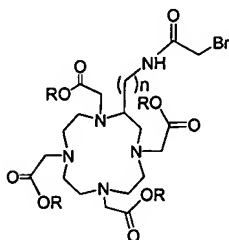
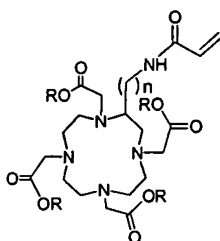
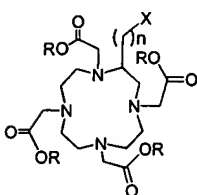
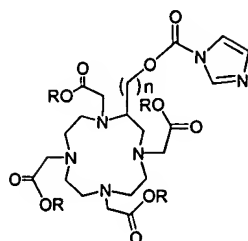
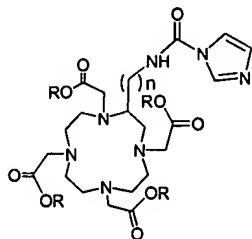
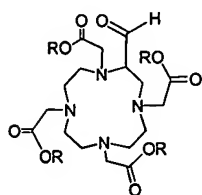
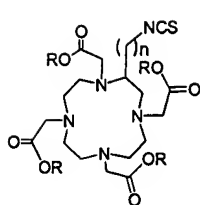
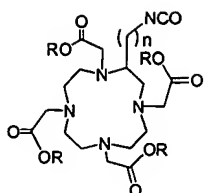
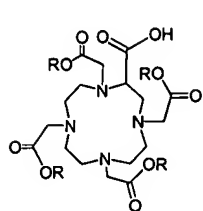
(e) transforming a plurality of the carboxylate precursor groups of the bound precursor chelate moiety to a plurality of carboxylate moieties, the carboxylate moieties capable of complexing a paramagnetic metal ion; and

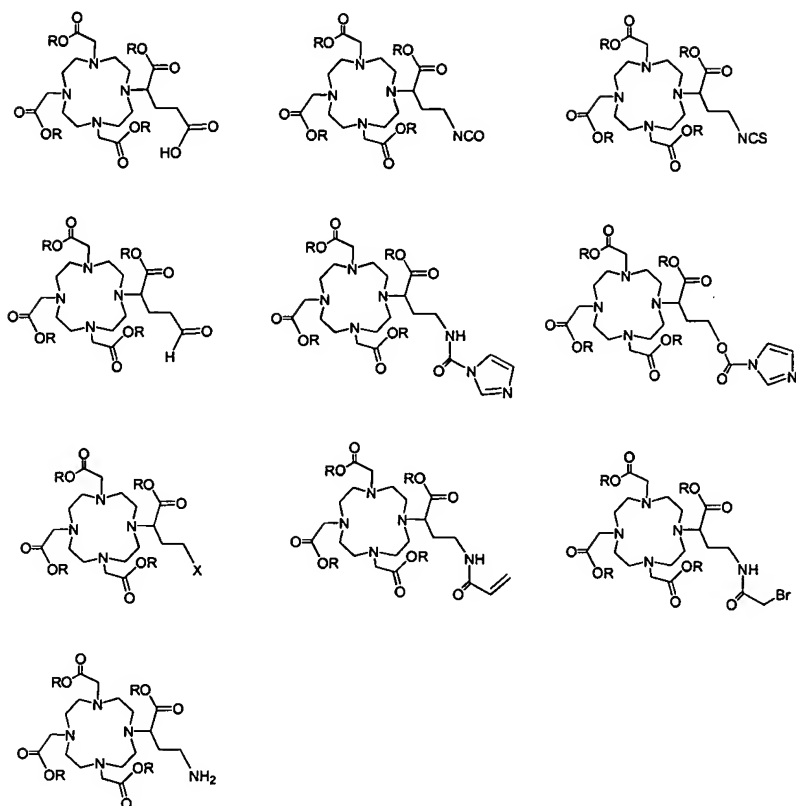
(f) complexing a paramagnetic metal ion to the plurality of carboxylate moieties to produce the MR imaging agent;

wherein the linker-subunit moiety is:



wherein the precursor chelate moiety is selected from the group consisting of:





and

wherein:

n is an integer from 1 to 4;

R is selected from the group consisting of a negative charge and a negative charge precursor capable of being transformed into a negative charge; and

X is a chemical leaving group selected from the group consisting of -Cl, -Br, -I, -MsO, -TsO, and -TfO; and

~~The method of claim 12 or 13,~~ wherein the negative charge precursor is selected from the group consisting of -H, -Me, -Et, -t-Bu, -benzyl, and -allyl.

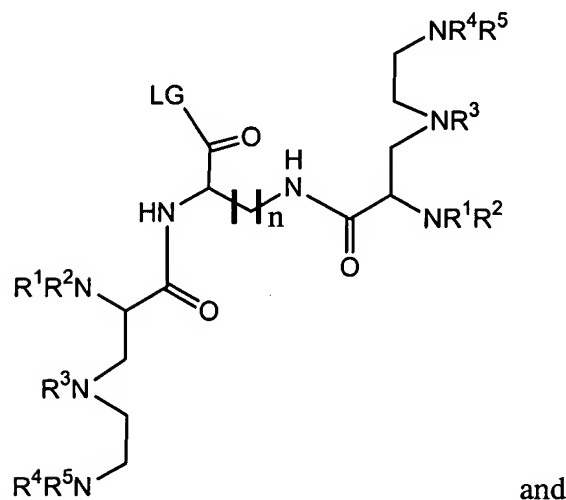
15. (Cancelled).

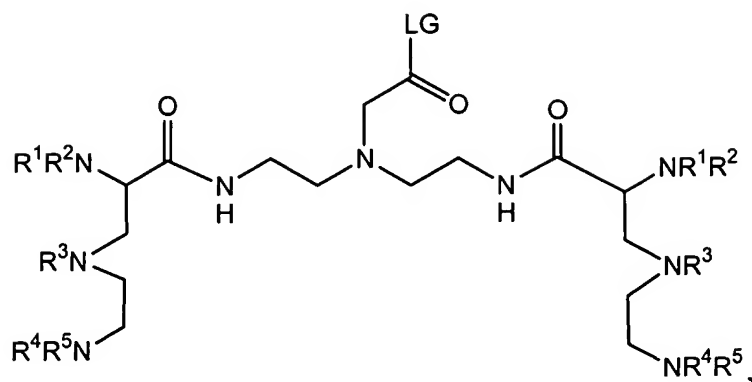
16. (Currently amended) A method of making an MR imaging agent, said method comprising:

c) converting the precursor MR imaging agent to the MR imaging agent;

NCC1=CC=CC=C1CN

~~The method of claim 15, wherein the covalent conjugate is selected from the group consisting of~~





wherein n is an integer from 1 to 4;

LG is a leaving group selected from the group consisting of -OH, activated ester, halide, and anhydride; and

R¹, R², R³, R⁴, and R⁵ are independently selected from the group consisting of an acetate moiety, a -Me, -Et, or -t-Bu protected acetate moiety, an acetamide moiety, and an acetoxy moiety.

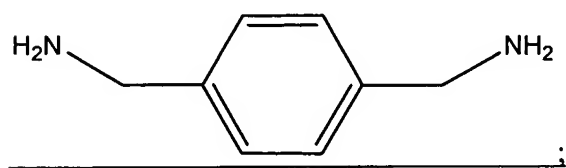
17. (Currently amended) A method of making an MR imaging agent, said method comprising:

a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;

b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent; and

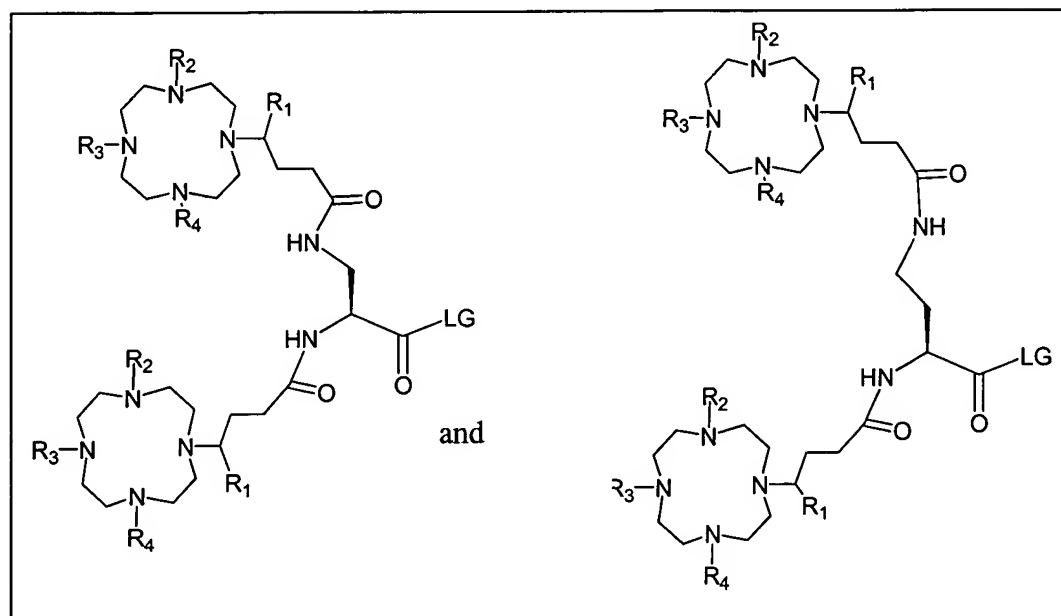
c) converting the precursor MR imaging agent to the MR imaging agent;

wherein the linker-subunit moiety is:



wherein the linker moiety is covalently conjugated to a precursor chelate moiety, the covalent conjugate comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;

~~The method of claim 15~~, wherein the covalent conjugate is selected from the group consisting of:



wherein:

LG is a leaving group selected from the group consisting of -OH, activated ester, halide, and anhydride; and

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are selected from the group consisting of an acetate moiety, a -Me, -Et, or -t-Bu protected acetate moiety, an acetamide moiety, and an acetoxy moiety.

18. (Cancelled).

19. (Currently amended) A method of making an MR imaging agent, said method comprising:

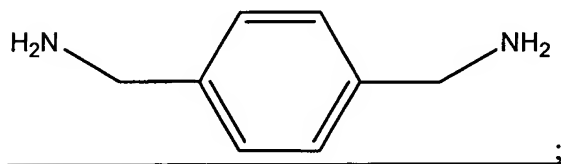


a) reacting a peptide having an N-terminal amine functional group with a linker-subunit moiety to form a modified peptide having a C-terminal amine functional group and said N-terminal amine functional group;

b) covalently attaching a linker moiety to the C-terminal amine functional group and to the N-terminal amine functional group to form a precursor MR imaging agent; and

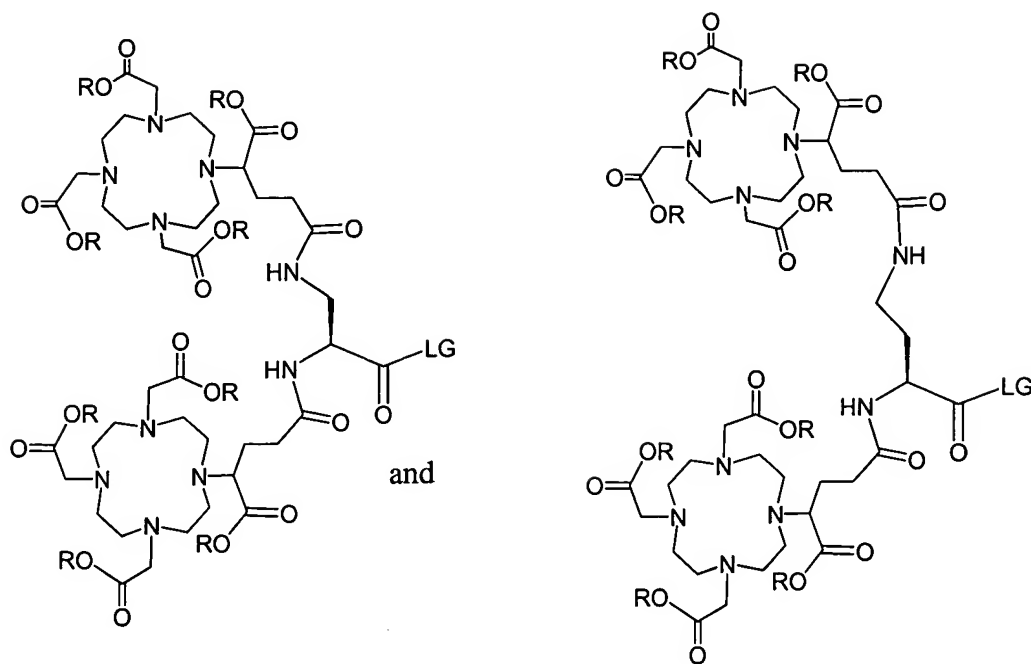
c) converting the precursor MR imaging agent to the MR imaging agent;

wherein the linker-subunit moiety is:



wherein the linker moiety is covalently conjugated to a precursor chelate moiety, the covalent conjugate comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties;

The method of claim 15, wherein the covalent conjugate is selected from the group consisting of:



wherein:

R is a -tBu group,

LG is a leaving group selected from the group consisting of -OH, activated ester, halide, and anhydride.

20. (Cancelled).

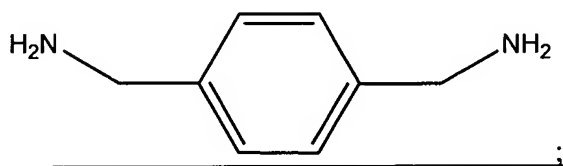
21. (Currently amended) The method of claim 11 or 14, ~~claim 8 or claim 20~~, wherein the paramagnetic metal ion is selected from the group consisting of: Gd(III), Fe(III), Mn(II and III), Cr(III), Cu(II), Dy(III), Tb(III and IV), Ho(III), Er(III), Pr(III), Eu(II) and Eu(III).

22. (Original) The method of claim 21, wherein the paramagnetic metal ion is Gd(III).

23. - 64. (Cancelled).

65. (Currently amended) A method for altering the stability of a peptide, the peptide having an N-terminal amine functional group, the method comprising:

a) reacting the peptide with a linker-subunit moiety to form a peptide having a C-terminal amine functional group, wherein the linker-subunit moiety is:



b) covalently attaching a linker moiety to the peptide's C-terminal amine functional group and N-terminal amine functional group to form a modified peptide;

c) reacting the modified peptide with a precursor chelate moiety to form a covalent bond between the precursor chelate moiety and the linker moiety of the modified peptide, the precursor chelate moiety comprising a plurality of carboxylate precursor groups, the carboxylate precursor groups capable of being transformed into carboxylate moieties; and

d) assaying the stability of the modified peptide and optionally comparing the stability of said modified peptide to the stability of said unmodified peptide;

~~The method of claim 59 or claim 60,~~ wherein the stability is assayed using a rat liver homogenate assay.

66. – 77. (Cancelled).